Coincidentally, we recently reported a study that analyzed the relationships between coronary stenoses and vessel structure assessed by CTA, PET-derived MFR, and cardiovascular risk factors (2). We showed that abnormal wall structure affects regional MFR beyond the presence and severity of coronary stenoses. Specifically, coronary calcium content was the main determinant of regional MFR and a significant predictor of depressed global MFR. Interestingly, when the Framingham risk score, an indicator of overall cardiovascular risk, was considered; it remained the only significant determinant of global MFR, beyond CTA variables.

Although the 2 investigations are similar with regard to baseline characteristics of patients and differ only slightly in their methodology, they come to apparently different conclusions. In our view, however, both studies point to the effects of diffuse coronary atherosclerosis, in addition to those of focal significant stenoses, on myocardial perfusion.

Accordingly, depressed regional MFR is closely linked to the coronary atherosclerotic burden in the related vessel, described by the "summed stenosis score" in the study by Naya et al. (1) and by the coronary calcium content in ours (2). Moreover, global MFR is consistently related to different indicators of cardiovascular risk, the Duke CAD index in the study by Naya et al. (1), and the Framingham risk score in ours (2).

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Reply

We appreciate the commentary by Drs. Liga and Neglia regarding the relationship between coronary anatomic features and quantitative myocardial flow reserve (MFR) as assessed by cardiac hybrid positron emission tomography/computed tomography. We agree that both studies consistently demonstrate that the total burden of atherosclerosis, quantified with coronary calcium score (1) or by the total stenosis score, which integrates the effects of serial plaques (2), contributes to downstream MFR more than stenosis severity alone. However, we would not characterize MFR as being "closely linked to atherosclerotic burden." Rather, both studies as well as other studies using invasive angiography (3) have demonstrated that the correlation between epicardial stenosis severity and quantitative measures of perfusion, although significant, is only modest in magnitude. This is likely due to the fact that anatomic descriptors of epicardial stenosis cannot capture the effects of diffuse atherosclerosis on vasodilator function of either the epicardial coronary arteries or the microvasculature. Nonetheless, we believe that both studies add valuable insights to the literature regarding the determinants and role of MFR, which will have increasing clinical application given its powerful prognostic significance (4).

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Limitations of Noninvasive Measurement of Fractional Flow Reserve From Coronary Computed Tomography Angiography

We read with interest the paper by Koo et al. (1) regarding the diagnostic accuracy of noninvasive measurement of fractional flow reserve (FFR) from coronary computed tomography angiography data (FFR_{CT}). We do recognize the potential clinical and economic relevance of the validation of a diagnostic tool able to noninvasively determine the presence of ischemia-inducing coronary lesions because it would dramatically reduce the number of diagnostic angiograms and guide subsequent coronary revascularization. However, we have some concerns regarding the interpretation of the results of the study.

First, the major potential drawback of FFR_{CT} relates to the fact that FFR is calculated during "simulated" and not "real" hyperemia. To this end, the authors assume that "microcirculation reacts predictably to maximal hyperemic conditions in patients with normal coronary flow." This sentence is substantiated by a bibliographic reference that demonstrates the reproducibility of the